CURRICULUM VITAE ROBERT BENJAMIN STEIN, M.D., PH.D.

DATE OF BIRTH:

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PLACE OF BIRTH:

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EDUCATION:

1968-72

Indiana University, Bloomington, IN, B.S. with distinction, May 1972

1972-79

Duke University Medical and Graduate Schools,

Durham, NC, 1972-1979

Ph.D. in Physiology & Pharmacology, December 1978

M.D., May 1979

BOARD CERTIFICATIONS:

Diplomate of the National Board of Medical Examiners

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North Carolina Permanent Medical License 25834

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Board certified in anatomic and clinical pathology,

December 1982

POSITIONS HELD:

1993-present

Senior Vice President

Chief Scientific Officer

Ligand Pharmaceuticals Incorporated

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1992-1993

Vice President, Research & Preclinical Development

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1990-1992

Vice President, Research

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1989-1990

Senior Director and Head

Department of Pharmacology

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1987-1989 Associate Director

Molecular and Cardiovascular Pharmacology

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Merck, Sharp, and Dohme Research Laboratories

1982-1987 Senior Research Fellow

Department of Virus and Cell Biology Research Merck, Sharp, and Dohme Research Laboratories

1979-1982 Resident, Department of Pathology

Duke University Medical Center

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National Merit Scholar

AWARDS AND HONORS:

1968-72

Indiana State Scholarship, (honorary) 1968-72 Phi Eta Sigma (freshman honorary) 1969 Phi Beta Kappa 1971 Bayard Floyd Microbiology Scholarship 1972 Alpha Omega Alpha (national medical honorary) 1975 National Institutes of Health Training Grant 1974-1975 Listed in Who's Who Among College Students 1976 James B. Duke Scholar 1976-1978

1977-1979 Insurance Medical Scientist Scholarship

1978 Sigma Xi

1979 Lange Medical Publications Award

PROFESSIONAL MEMBERSHIPS:

American Society of Clinical Pathologists

American Association for the Advancement of Science

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September 16, 1993

ADDITIONAL PROFESSIONAL RESPONSIBILITIES, MSDRL:_

Chairman, Cancer Technology Assessment Group

Chairman, Cardiovascular and Ion Channel Matural Products Screening Group

Co-chairman, Ion Channel Working Group

Member, Research Coordinating Compattee

Member, Merck / DuPont Angiotens II Receptor Antagonist Discovery Team

Member, Promotion Peer Review Committee

Member, Cardiovascular Technology Assessment Group

Member, Natural Products Task Force Steering Committee

Member, Molecular Biology Steering Committee

Member, Transgenic Animal Steering Committee

Member, Nuclear Imaging Technology Assessment Group

Member, Fibrinolysis Working Group

Member, Fibrinogen Receptor Antagonist Working Group

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ADDITIONAL PROFESSIONAL RE

PUBLICATIONS:

- 1. Borowitz, M.J., R.B. Stein, and J.J. Blum. 1977. Quantitative Analysis of the Change of Metabolite Fluxes Along the Pentose-Phosphate and Glycolytic Pathways in *Tetrahymena* in Response to Carbohydrates. J. Biol. Chem. 252: 1589-1605.
- 2. Stein, R.B. and J.J. Blum. 1978. On the Analysis of Futile Cycles in Metabolism. J. Theoret. Biol. 72: 487-522.
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- 4. Stein, R.B. and J.J. Blum. 1980. Quantitative Analysis of Intermediary Metabolism in *Tetrahymena*: Cells Grown in Glucose-Supplemented Medium. J. Biol. Chem. 255: 4198-4205.
- 5. Stein, R.B. and J.J. Blum. 1981. Quantitative Analysis of Intermediary Metabolism in *Tetrahymena*: Cells Kept Under Static Conditions for 4 Hours After Growth in Glucose-Supplemented Medium. J. Biol. Chem. 256: 2752-2760.
- 6. Blum, J.J. and R.B. Stein. 1982. "On the Analysis of Metabolic Networks" in *Biological Regulation and Development*, Vol. 3A, pp.99-125, R. Goldberger, ed., Plenum Press, New York.
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- 8. Stein, R.B. and J.L. Linder. 1984. "Mononuclear Leukocytosis and Infectious Mononucleosis" in Laboratory Hematology, pp. 189-228, J. Koepke, ed., Churchill Livingstone, Inc., New York.
- 9. Giangaspero, F., P.C. Burger, D.R. Osborne, and R.B. Stein. 1984 Suprasellar Squamous Epithelioma: "Papillary Craniopharyngioma". Am. J. Surg. Pathol. 8(1): 57-64.
- 10. Borowitz, M.J. and R.B. Stein. 1984. Special Article: Diagnostic Applications of Monoclonal Antibodies to Human Cancer. Arch. Pathol. & Lab. Med. 108: 101-105.
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- 15. Preiss, J., C. Loomis, R.B. Stein, J. Niedel, and R.M. Bell. 1986. Quantitative Measurement of s,n-1,2-Diacylglycerols Present in Platelets, Hepatocytes and *ras* and *sis*-transformed Normal Rat Kidney Cells. J. Biol. Chem. 261(19): 8597-8600.
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- 19. Wegrzyn, R.J., D. Defeo-Jones, D. Heimbrook, J. Wallen, D. Kiefer, R.B. Stein, M.W. Riemen, and A. Oliff. 1989. Spontaneously Transformed NRK Cells Lose Their Mitogenic Response to Epidermal Growth Factor. Growth Factors 1: 227-236.
- 20. McClements, W., G. Yamanaka, V. Garsky, V. Perry, S. Bachetti, R. Colonno and R.B. Stein. 1988. Oligopeptides Inhibit Herpes Simplex Virus Ribonucleotide Reductase by Inducing Subunit Dissociation. Virology 162:(1)270-273.
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- 23. Winquist, R.J., L.A. Heaney, A.A. Wallace, E.P. Baskin, R.B. Stein, M.L. Garcia, and G.J. Kaczorowski. 1989. Glyburide Blocks the Relaxation Response to BRL 34915 (Cromakalim), Minoxidil Sulfate and Diazoxide in Vascular Smooth Muscle. J. Pharmacol. Exper. Therapeut. 248(1): 149-156.
- 24. Lynch, J.J., L.A. Heaney, A.A. Wallace, J.R. Gehret, H.G. Selnick, and R.B. Stein. 1990. Suppression of Lethal Ischemic Ventricular Arrhythmias By the Class III Agent E4031 in a Canine Model of Previous Myocardial Infarction. J. Cardiovasc. Pharmacol. 15(5):764-75.

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- 36. Dawson, M. I., Hobbs, P.D., R.B. Stein, Berger, T.S., Heyman, R.A. 1992. Interaction of Retinoids with Retinoic Acid Nuclear Receptor Isoforms. Retinoids Progress in Research and Clinical Applications, M.A. Livrea and L. Packer (eds.), Marcel Dekker, Inc., New York, pp. 205-221.
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ABSTRACTS:

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- 3. Stein, R.B., M. Lasecki, B.P. Croker, and W.W. Johnston, 1982. Immunological Detection of Keratin in Respiratory Cytologic Material. Acta Cytologica 26(5): 727.
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- 5. Stein, R.B. Expression of Viral Harvey *ras* p21 in *E. coli* and Photoaffinity Labeling with GTP. Presented at Gordon Conference on Animal Cells and Viruses, August 1983.
- 6. Gibbs, J., R. Ellis, I. Sigal, R.B. Stein, M. Poe, and E.M. Scolnick. Autophosphorylation of v-Haras p21 is Modulated in Whole Cells and *in vitro* by Amino Acid Residue 12. Cold Spring Harbor RNA Tumor Viruses Meeting, May 1984.
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- 8. Poe, M., E.M. Scolnick, and **R.B. Stein**. 1985. HPLC Analysis of Guanine-Nucleotide Content of Purified Viral Harvey *ras* p21 Expressed in *E. coli*. Fed. Proc. 44(4): 1209.
- 9. Storer, R.D., R.B. Stein, J.F. Sina, J.G. DeLuca, H.L. Allen, and M.O. Bradley. 1986. Malignant Transformation of a Preneoplastic Hamster Epidermal-Cell Line by the EJ c-Ha-ras Oncogene. J. Cell. Biochem. S10A: 27.
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- 11. Stein, R.B., J.Y. Tai, and E.M. Scolnick. Molecular Cloning of the Temperature Sensitive 371 Kirsten Murine Sarcoma Virus and Expression in *E. coli* of the Mutant and Wild Type Viral Kirsten *ras* p21 Proteins, Cold Spring Harbor RNA Tumor Virus Meeting. May 1986.
- 12. McClements, W.M., G. Yamanaka, V. Garsky, H. Perry, S. Bacchetti, R. Colonno, and R.B. Stein. Oligopeptides Inhibit Herpes Simplex Virus Ribonucleotide Reductase by Inducing Subunit Dissociation. 12th International Herpesvirus Meeting. 1987.

 ABSTRACTS (continued)
- 13. Lynch, J.J., L.A. Heaney, A.A. Wallace, and R.B. Stein. Suppression of Lethal Ischemic Ventricular Arrhythmias by the Class III Agent E4031 in a Canine Model of Previous Myocardial Infarction. International Society for Heart Research, American Section, Ann Arbor, MI, May 14-18, 1989.
- 14. Swanson, R., J. Antanavage, R.B. Stein, M. Tanouye, and J.S. Smith. Chimeric Shaker cDNA transcripts induce the expression of kinetically distinct K⁺ currents in *Xenopus*. Biophysical Society Meeting, Cincinnati, OH, February 12-16, 1989.
- 15. Lynch, J.J., L.A. Heaney, A.A. Wallace, J.R. Gehret, J.R., and R. B. Stein. Failure of Lidocaine to Prevent Lethal Ischemic Ventricular Arrhythmias in a Canine Model of Previous Myocardial Infarction. American Heart Association, New Orleans, LA, November 13-16, 1989.

- 16. Folander, K., J.S. Smith, J. Antanavage, C. Bennett, J. Williams, L. Kaczmarek, L., R.B. Stein, and J. Smith. Cloning and Expression of Delayed Rectifier K* Channels from Neonatal Rat Heart and DES primed Rat Uterus. American Heart Association, New Orleans, LA, November 13-16, 1989.
- 17. Swanson, R., K. Folander, J. Antanavage, C. Bennett, J. Williams, L. Kaczmarek, L., R.B. Stein, and J. Smith. Cloning and Expression of K+ Channels from Rat Brain. American Heart Association, New Orleans, LA, November 13-16, 1989.
- 18. Lynch, J.J., R.T. Wiedmann, E.P. Baskin, L.A. Heaney, R.B. Stein, and H.P. B., Cingolani, Contractile Behavior of the Novel Class III Antiarrhythmic Agent. American Heart Association, New Orleans, LA, November 13-16, 1989.
- 19. Luneau C.J., J.B. Williams, and R.B. Stein. Age and Tissue-Related Expression of Potassium Ion Channel mRNA Levels in the Rat. American Heart Association, New Orleans, LA, November 13-16, 1989.
- 20. Buhrow, S., R. Swanson, K. Folander, C. Luneau, J. Antanavage, C. Bennett, J. Williams, L. Kaczmarek, R.B. Stein, and J. Smith. Cloning and Characterization of Delayed Rectifier K* Channels from Rat Brain. Nucleic Acid Technologies Meeting, Albany, NY, September 21-24, 1989.
- 21. Swanson, R., K. Folander, J. Antanavage, C. Bennett, J. Williams, L. Kaczmarek, R.B. Stein, and J. Smith. Cloning and Expression of K⁺ Channels from Rat Brain. Society for Neurosciences Annual Meeting, Phoenix, AZ, October 29 November 3, 1989.
- 22. Folander, K., J. Smith, J. Antanavage, C. Bennett, R.B. Stein, and R. Swanson. Cloning and Expression of K⁺ Channels from Neonatal Rat Heart and DES-Primed Rat Uterus. Society for Neurosciences Annual Meeting, Phoenix, AZ, October 29- November 3, 1989.
- 23. Bednar, D.L., R.B. Stein, V.M. Garsky, and D.L. Williams. Apparent Molecular Weight of the Endothelin Receptor, 34th Annual Meeting of the Biophysical Society, February 18-22, 1990.

ABSTRACTS (continued):

- 24. Swanson, R., K. Folander, C. Bennett, C., J. Antanavage, J., R.B. Stein, and J. Smith. Total Synthesis, Expression, and Functional Assay of a Gene Encoding a Human Delayed Rectifier potassium Channel, 34th Annual Meeting of the Biophysical Society, February 18-22, 1990.
- 25. Williams, J., C. Luneau, R. Swanson, K. Folander, C. Bennett, J. Antanavage, L. Kaczmarek, R.B. Stein, and J.S. Smith. Cloning and Expression of a Genomic DNA Clone Encoding a Rat Brain Potassium Channel. 34th Annual Meeting of the Biophysical Society, Baltimore, MD, February 18-22, 1990.
- 26. Smith, J.S., R.B. Stein, and R. Swanson. Kinetics of cloned K⁺ currents change with level of expression in *Xenopus* oocytes. 34th Annual Meeting of the Biophysical Society, Baltimore, MD, February 18-22, 1990.

- 27. Baskin, E., C. Serik, A. Wallace, L. Brookes, D. Claremon, H. Selnick, R.B. Stein and J. Lynch. Comparative effects of Class III antiarrhythmic agents on refractoriness in isolated ventricular myocardium. Federation of American Societies for Experimental Biology Annual Meeting, Washington, DC, April 2-5, 1990.
- 28. Stupenski, R., A. Wallace, L. Brookes, D. Claremon, H. Selnick, R.B. Stein, and J. Lynch. Cardiac electrophysiologic and hemodynamic effects of Class III antiarrhythmic agents in anesthetized dogs. Federation of American Societies for Experimental Biology Annual Meeting, Washington, DC April 2-5, 1990.
- 29. Serik, C., E. Baskin, R. Wiedmann, L. Brookes, D. Claremon, H. Selnick, R.B. Stein, and J. Lynch. Inotropic effects of Class III antiarrhythmic agents in isolated ventricular myocardium. Federation of American Societies for Experimental Biology Annual Meeting, Washington, DC, April 2-5, 1990.
- 30. Wallace, A., J. Gehret, L. Heaney, R. Stupienski, R.B. Stein, and J. Lynch. Failure of lidocaine to prevent lethal ischemic ventricular arrhythmias in a canine model of previous myocardial infarction. Federation of American Societies for Experimental Biology Annual Meeting, Washington, DC, April 2-5, 1990.
- 31. Folander, K., J. Smith, R.B. Stein, and R. Swanson. Cloning of K^+ Channels Underlying the Cardiac I_K Current. International Soc. for Heart Research, Chicago, IL, May 8-11, 1990.
- 32. Williams, J., C. Luneau, R. Swanson, K. Folander, J. Antanavage, C. Bennett, L. Kaczmarek, R.B. Stein, and J.S. Smith. Cloning and Expression of a Genomic DNA Clone Encoding a Rat Brain Potassium Channel. Biophysical Society Meetings, Washington, DC, February 1990.

ABSTRACTS (continued):

- 33. Total Synthesis, Expression, and Functional Assay of a Gene Encoding a Human Delayed Rectifier Potassium Channel. Biophysical Society Meeting, Washington, DC, February 1990.
- 34. Folander, K., Lin, C.S., Smith, J.S., Swanson, R., and R.B. Stein. Cloning of Potassium Channel Complementary DNA from Rat Leukocytes and Human T Cells. Society for Neurosciences Annual Meeting, St. Louis, MO, October 28-November 2, 1990.
- 35. Luneau, C.J., Buhrow, S.A., Marshall, J., Antanavage, J., Levitan, E., Smith, J., Swanson, R., Folander, K., Bennett, C., R.B. Stein, et al. Cloning and Expression of K-V4 A Rat Brain Delayed Delayed Rectifier Potassium Ion Channel Complementary DNA. Society for Neurosciences Annual Meeting, St. Louis, MO, October 28-November 2, 1990.
- 36. Elliott, J.M., Baldwin, J.J., Buhrow, S. A., Claremon, D.A., Lynch, J.J., Ponticello, G.S., Radzilowski, E.M., Remy, D.C., Selnick, H.G., R.B. Stein, et al. Benzopyranone Spiropiperidines as

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37. McDonnell, Donald P., Dana, Sharon L., Hoener, Patricia A., Lieberman, Benjamin A., Imhof, Markus O., and R.B. Stein. Cellular Mechanisms Which Distinguish between Hormone- and Antihormone- Activated Estrogen Receptor. New York Academy of Sciences conference, Steroid Receptors and Antihormones, Dallas, Texas, September 20-23, 1994.

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- 1. United States Patent 4,814,432, Inhibitor of Ribonucleotide Reductase, Inventors: Roger Friedinger, John Hannah, Victor M. Garsky, Robert B. Stein, Richard L. Tolman, March 21, 1989.
- 2. United States Patent 4,837,304 Inhibitor of Ribonucleotide Reductase, Inventors: Victor M. Garsky, Robert B. Stein, Richard L. Tolman, July 4, 1989.
- 3. International Application Number PCT/US92/07064, Use of Selective Ligands for Treatment of Hormone Responsive Disease States, Ronald M. Evans, Richard A. Heyman, Christina S. Berger, and Robert B. Stein, August 21, 1992.
- 4. United States Patent Application Serial Number 07/872,710, Non-Steroid Progesterone Receptor Agonist and Antagonist Compounds and Methods, Inventors: T. S. Berger, W. Fenical, C. Pathirana, and Robert B. Stein. September 8, 1992.
- 5. United States Patent Application Serial Number 08/048,646, Non-Steroid Progesterone Receptor Agonist and Antagonist Compounds and Methods, Inventors: T. S. Berger, W. Fenical, C. Pathirana, Robert B. Stein, T. Jones, L. Hamann, and L. Farmer, April 16, 1993.